Review Articles

The feasibility of establishing classification system for ovarian function

Wei Wang[1], Yan-Qing Wang[1], Ying-Ying Qin[2], Yu-Jie Dang[2], Ming-Di Xia[2], Ying Ma[3], Yu-Lan Mu[4]

[1] Department of Ultrasonic Diagnosis & Treatment, Shandong Provincial Hospital Affiliated to Shandong University, Jinan
[2] Reproductive Hospital Affiliated to Shandong University, Jinan; [3] Medical College of Qingdao University, Qingdao
[4] Department of Obstetrics & Gynecology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan (China)

Summary

The occurrence, development, and decline of ovarian function are the foundation in women's whole life stages, which reflect the process beginning from embryo formation to the aging. Correct assessment of ovarian function is significant for evaluating the potential reproductive ability and predicting the age of menopause, as well as providing both individualized and proper treatment and preventive care based on physiological characteristics of women in different phases. Ovarian reserve (OR) is used to predict the potential fertility of women by evaluating the follicles and the quantity and quality of eggs. Currently, there are multiple indexes used to evaluate ovarian reserve, including anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), estradiol (E2), inhibin B, antral follicle count (AFC), etc. Although some scholars combine multiple indexes to evaluate the ovarian function, these indexes are far less accurate, detailed, and comprehensive. To find an ideal method for evaluation of ovarian reserve is the hotspot in research of reproductive endocrine. The present authors, for the first time, put forward a classification system of ovarian reserve function after summarizing numerous cases. It can both accurately and effectively evaluate the ovarian function quantitatively. It is of great help in making clinical decisions and of great significance in future development.

Key words: Ovarian reserve; Anti-Müllerian hormone (AMH); Inhibin B (INH B); Antral follicle count (AFC); Follicle stimulating hormone; Estradiol.

Introduction

Ovary is a sexual organ generating and discharging ovum, as well as secreting steroid hormone. The occurrence, development, and decline of ovarian function are the foundations in women's whole life stages, which reflect the process beginning from the embryo formation to aging. Correct assessment of ovarian function is significant for evaluating the potential reproductive ability and predicting menopause age, as well as providing both individualized and proper treatment and preventive care, which is based on the physiological characteristics of women in different phases. However, so far there has been no reliable methods for evaluating the degree of aging of ovary.

Ovarian reserve (OR), a method relatively accurate at present, is used to predict the potential fertility of women by evaluating the follicles and the quantity, quality of eggs. Currently, there are multiple indexes used to evaluate ovarian reserve, including anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), estradiol (E2), inhibin B, antral follicle count (AFC), etc. Although some scholars combine multiple indexes to evaluate the ovarian function, these indexes are far less accurate, detailed, and comprehensive. Finding an ideal method for evaluation of ovarian

reserve is the hotspot in research of reproductive endocrine. The present authors, for the first time, put forward a classification system for ovarian reserve function after summarizing numerous cases. It can both accurately and effectively evaluate the ovarian function quantitatively. It is of great help in making clinical decisions and of great significance in future development.

Review

There are multiple indexes already used to evaluate ovarian reserve, wildly recognized by most of the researchers in reproductive endocrinology. The currently utilized indexes and their application values are mentioned below after comprehensive analysis of documents.

Age

Age is a factor that has extremely intimate relationship with fertility. The older a woman becomes, the greater the incidence of infertility becomes, and thus fertility competence reduces along with age. It will lead to the decreasing rate of pregnancy and increasing rate of abortion, prolonged average interval between bearing and higher odds of ab-

normal chromosome in next generations, as well as descending live birth rate. It was recorded that the fertility ability of women begins to decrease near the age of 30 years and dramatically decreases at the age of 38 years thereafter towards menopause. This phenomenon is called folded stick mechanism [1]. According to (WHAS11), 90 percent of follicles have been lost by the age of 30, and only three percent of them still exist at 40 years. Recently, researchers found that serum AMH decreased by a rate of 5.6% every year, and the decreasing rate for AFC (2~10 mm) was 4.4%, for the volume of ovary it was 1.1%. There is an evident negative correlation between the age of women and the level of serum AMH, AFC, and the volume of ovary. It has also been found that the proportion of small follicles in ovary (2~4 mm) gradually decreased as the age increases, whereas no obvious changes were seen in the proportion of medium and large follicles, which had the reversed tendency compared with the small follicle. It is rather conspicuous that the increase proportion of large follicle is related to the decreasing level of serum AMH and overall level of AFC. Compared with the actual biological age of women, the age of ovary has stronger connection with the quantity of large follicle given the statistics of AMH and AFC. In other words, it is inaccurate to judge OR merely by the age and the synergy of AMH and AFC has relatively higher accuracy to help predict OR [2].

Ovarian changes and evaluation of ovarian function

The first clinical representation of reproductive senility is the shortened menstrual cycle. Irregular menstrual cycle is the beginning sign of menopausal transition. Stages of reproductive workshop (STRAW) is the first international standardized staging system [3], however, it is restrained only in the changes of menstruation and does not take other influential factors into account, not to mention other prerequisites for this system, such as "only suitable for women older than 40 years with a body mass index (BMI) < 18 or > 30, women without smoking habit and chronically irregular menstruation only, "women with excision of uterus or abnormal anatomy of ovary and uterus are not compatible". An ideal staging system ought to indicate the normal pattern of menopausal transition, and roughly estimate the time before the final menstrual period, and eventually indicate a warning point (or phase) incorporating other factors like hormones. The standard for this system should be objective, reliable, economical, and convenient, while offering promising prospective and clear boundary. In addition to the aforementioned requirements, cohort studies and statistical analysis validation are also waiting to be implemented, given that the standard of STRAW system is just a consensus for now.

There was a research conducted in 2005, studying the changes of menstruation of middle-aged females in England and measuring the daily discharge amount of four urinary reproductive hormones. It was of significant advancement in this research not only because of the observation in the changes of menopausal transition, but also for the adding of the observation in the changes of sexual hormone. It fully revealed the variation rules of menstrual cycle and reproductive hormones during late period of childbearing, early, and late stages of menopausal transition, so as to help us accurately understand the complexity in the changes of normal menstruation. The present author highly recommends the large sample research conducted by Professor Lin Shouqing, whose student He Zhong published his doctoral dissertation in 2008: "The reminder value of the changes in menstruation to the process of decline of ovarian function", which proved that the STRAW system can be an accurate indicator for the decline of ovarian function, meanwhile, possessing the disadvantages of incomprehensive staging, unable to reflect endocrine function, especially changes in FSH and AMH. Overall, the change of menstruation is an issue with complex manifestation and difficult statistics.

After a series of clinical and endocrine research, there are four stages generally recognized in the women's reproductive decline: 1) increasing level of FSH in early follicle phase signals the beginning of reproductive decline; 2) emergence of irregular menstrual cycle indicates the beginning of menopausal transition (MT); 3) absence of periodical pattern in ovarian activity, occasionally, fluctuation of E2 and subsequent uterine bleeding can be expected; 4) cease of ovarian function. The level of FSH and LH continue to upsurge and that of E2 and progesterone continue to drop, indicating menopause. The introduction of new developments in the field of immunology and genetics are conducive to the understanding of the occurring mechanism of ovarian decline, as well as guide clinical work much more efficiently [4].

Hormone and cytokines and the functional evaluation of OR

AMH

The change in AMH levels has been found to be an index that both sensitively and stably assess the function of OR in recent years, it is of unparalleled significance and clinical value. AMH is secreted by the granular cells in pre-antral follicle and small antral follicle, acting during the period when primordial follicle converts to growing follicle, and during the collection of FSH-sensitive follicle in early antral follicle stage. It either directly or indirectly influences the development process of follicle by exerting on AMH receptor, and is capable of inhibiting the growth of follicle and preventing the follicle from growing too rapidly and untimely depleting, and thus has the ability to reserve OR.

Compared with the variation of AFC, there is no significant variation of AMH among different periods of relatively stable menstrual cycles [5, 6], for which characteristic could make AMH a much more convenient

clinical marker compared to AFC, basic FSH level and the ratio of FSH/LH, it also can be measured randomly in one menstrual cycle and free from the restriction of the cycle [7-10]. However, according to the recent studies in which 82 serum samples of 12 women with regular OR underwent serological testing, indicated that there were changes in AMH during the different stages of menstrual cycle. Peak average concentration of serum AMH was 7.9 pmol/L and minimum value was 6.7 pmol/L [11].

According to other researches, there was a downward trend for AMH along with the increase of age. There is a swift drop between 30 and 40 years of age, after which it decreases more gradually. AMH cannot be traced in the women with premature ovarian failure (POF) or menopause [12, 13]. Tremellen *et al.* [14] observed the level of serum AMH in 238 women ranging from 18 to 46 years of age, with a FSH all below ten U/L. They found that the level of AMH could be maintained at a relatively balanced level of 20~25 pmol/L for women between age of 18 to 29, and began to drop after age 30, reaching ten pmol/L at the age of 37. Surprisingly, no evident change of AMH levels was found between 29 and 37 years of age.

In conclusion, AMH can be used as an ideal index for evaluating ovarian function, foreseeing the decline of ovarian function and predicting the age of menopause [15, 16]. AMH < 0.8 ng/ml can be viewed as severe deficiency of OR. Gnoth *et al.* [17] studied the indicative effect of AMH on the decline of ovarian function, finding that if they regarded 1.26 ng/ml as the cut-off point, the predictable OR had a decreasing rate of 97% and the hypoergia of ovary could be 88%.

The level of serum AMH not only can be of great importance for evaluating ovarian function, but also can be a brilliant prophet to one's fertility. Yarde *et al.* [18] found that the level of AMH had a clear correlation with live birth rate, especially for low-fertility women with increasing FSH. For this reason, it can be an important index for predicting actual fertility. Whereas the other experiments of predicting OR and biological age have restrained value in predicting live birth rate. The live birth rate of the woman with serum AMH above 5.7 ng/ml is 3.18 times of that of others. Regression analysis showed that AMH is a reliable factor to predict IVF [19].

It would be a more reliable index to predict OR if we combined AMH and AFC. The patients with poor ovary response or with no response tend to have high cycle cancellation rate (>22%) and low rate of pregnancy (poor response: 6.7% and no response: 9.8%) [20]. The level of serum AMH is closely related to the number of primordial follicle in ovary, (r = 0.72); there still exists a significant connection between them even after adjustment of age factor (r = 0.48) [21]. Moreover, women with polycystic ovary syndrome (PCOS) have a higher level of serum AMH than healthy one do. For women between 29~38 years of age, the sensitivity and specificity of PCOS is 74% and 79%, as relatively indicated by AMH level and the cut-off value is 3.5 ng/ml [12].

INH B

INH B is an important dimer glycoprotein hormone, which belongs to transforming growth factor (TGF) β superfamily. It is mainly secreted by the ovarian granular cells. The principal factor relevant to reproduction is INH, and the subunit of β can be divided into two types: INH A and INH B. INH B is produced by the small primary follicle and secondary follicle, and there is a positive correlation between small AFC in ovary and the basis INH B, whose concentration in serum can reflect the quantity and quality of follicles. In the normal menstrual cycle, INH B reaches its peak in the early or middle follicular phase; selective feedback inhibits the synthesis and secretion of FSH in anterior pituitary, as well as blocks the hypothalamus GnRH so as to stimulate the release of hypophysis FSH. It has a strong negative effect on the secretion of FSH and is good for the maturation of follicle. When OR decreases, INH B produced by granular cells begins to reduce at first; feedback mechanism results in the increase of gonadotropin hormone (GTH), and the decrease of INH B occurs before the increase of FSH and E2. As a result, INH B can be more sensitive than basis FSH and E2 in predicting the function of OR. When INH B ≤ 45 pg/ml, the sensitivity regarding its prediction of low reaction of ovary is 92.9%, and its specificity is 97.4%. Positive predictive value is 86.7%, indicating a drop of OR [22].

There also exists a significant correlation between AFC and the level of serum INH B (r=0.40) [21]. The level of serum INH B is able to reflect fertility as well. Several studies had shown that fertility dropped along with the decreasing level of INH B [19].

Baseline FSH (bFSH)

bFSH (between the second and third day in menstrual cycle) is a commonly used index to evaluate the function of OR. Clinically, FSH ≥ 15~20 mIU/ml is a criteria of low ovarian function [4]. Other hormones like E2, P, LH, etc, also become modified but later than the upsurge of FSH, and their boundary is also ambiguous. Therefore, the change in the FSH leve is an outstanding marker to evaluate the decline of ovarian function. The upsurge of FSH is the early sign of anovulation of ovary and decreasing OR functions. Early studies thought that when bFSH ≥ 15I U/L, the cycle cancellation rate increased, and the peak value of E2 at injection day, collectable follicles, the number of transplanted embryos, and the rate of pregnancy became obviously decreased. The level of serum FSH showed a close relationship with primordial follicle count (r = 0.32) [21].

FSH/LH (luteinizing hormone)

The value of FSH/LH has been valued as an index to evaluate the decrease of OR in clinic [23, 24]. Barroso *et al.* found that patients with FSH/LH > 3.0 had significantly fewer mature oocytes and lower implantation and pregnancy rates than patients with FSH/LH < 3.0 [25]. Peng *et*

al. [26] thoroughly discussed the connection among 2,721 cycles of FSH/LH values and the consequence of controlled ovarian hyperstimulation (COH), finding that FSH/LH > 2 always means unsatisfied result of patient reacting COH. Lin *et al.* [27] assessed the value of FSH/LH in normal FSH women, similarly, they found that the ovarian reaction with FSH/LH > 2 was inferior to that of FSH/LH < 1. Shrim *et al.* [28] conducted a research in patients under age of 41 and with FSH < 8 IU/L, and found that the peak value of E2, the number of obtained eggs and the rates of fertilization and pregnancy was higher than that in the control group. Hence the value of FSH/LH can be used as an index to evaluate ovarian reaction.

Level of E2

Serum E2 mainly derives from granular cells and directly reflects follicular development. Certain E2 levels will guarantee the activation of the hypothalamus-hypophysis-ovary axis, however, an upsurge of basis E2 often indicates the drop of OR. Scientists originally thought that when the basis E2 ≥ 45 pg/ml, OR, the number of developing follicle, the rate of harvesting eggs, pregnancy and fertilization rates were all reduced. It was very difficult to achieve a pregnancy when basis E2 ≥ 75 pg/ml. The cycle cancellation rate could be 33% when E2 ≥ 80 pg/ml, which impeded pregnancy. However according to other reports, there was no evident change in the level of E2 between pregnant and non-pregnant groups.

Smotrichtm *et al.* [29] proved that regardless of FSH level, fertility could be determined to be low when E2 ≥ 80 pg/ml at the third day of the menstrual cycle. During the process of ovulation induction, the cycle cancellation rate will increase because of low or null reaction of ovary. When E2 ≥ 100 pg/ml, cancellation rate was higher showing worse reaction of ovary. Frattraelli *et al.* [30] observed 2,634 women, whose E2 levels were either < 20 pg or >100 pg/ml. They separated groups every 10 pg/ml and observed the rate of obtaining eggs, pregnancy, and cycle cancellation. Finally, they reached the conclusion that when E2 < 20 pg/ml or > 80 pg/ml, cycle cancellation rate became obviously increased. It could predict E2 level in women older than 40 years; however, in woman with no cycle cancellation, E2 cannot predict their ovarian reaction and rate of pregnancy.

Ultrasonic testing of ovary and evaluation of ovarian function

Assessing OR by ultrasonography is being increasingly applied for its unparalleled advantages, such as free from trauma, repeatability, and so on. The major processes include assessing AFC, calculating ovarian volume (OVVOL), and stromal blood flow. Antral follicle is the precursor of mature follicle and is a follicle with the diameter of two to ten mm by ultrasound. As the development of follicle does not rely on GnRH stimulation during early stage of antral follicle, large amounts of AFC whose number can perfectly reflect the remnant primordial follicles in the follicle pool, will be mature after enough stimulation by GnRH [31]. With regards to the selection of AFC threshold point, reports have incongruous results. According to Frattarelli *et al.* [32], patients with AFC ≤ ten had low reactivity towards Gn stimulation and increasing rate of cycle cancellation, but nothing changed in the rate of pregnancy. However in the study of Ng *et al.* [33], the cycle cancellation rate was 3.8% and 9.1% when AFC ≤ nine and AFC ≤ six. According to Saleh *et al.* [34], patients with AFC ≤ ten required extra days of stimulation and increased amounts of Gn. Their rates of pregnancy were still low. Domestic study used long protocol to retrospectively analyze 5,865 cases of IVF/ICSI-ET, and indicated that AFC was a good indicator to evaluate OR function, and was better in predicting ovarian reactivity than predicting the result of IVF [35].

Chen *et al.* [36] believed that for women whose AFC ≤ ten with an age older than 38 or whose AFC ≤ seven could be viewed as the threshold for evaluating the decline of OR. Other scientists defined the types of ovary by the amount of AFC (unilateral), less than five meant decline of OR, 5~12 follicles indicated normal, and higher than 12 was considered polycystic ovary. AFC with 2-6 mm diameter could be more effective to reflect OR [37]. The small follicle (2~4 mm) reduced along with increase of age, no evident changes for middle follicle (5~7 mm), and the large follicle (8-10 mm) increased along with the increase of age. The increasing proportion of large follicle is closely related to the reduced AMH and overall AFC [38]. AFC and the number of primordial follicle have significant correlation with each other (r=0.78). There still exists significant connection between them even after adjustment for age factor (r=0.53) [21].

It was reported that the predictive value of AMH and AFC exceeded that of FSH, E2, and INH B [19]. AUC was 0.935 and 0.905, respectively; the sensitivity was 93% for AFC evaluating low reaction of ovary and specificity was 88%, AMH sensitivity was 100%, and specificity was 73% [2], In addition, AFC is a reliable factor to evaluate live birth rate of IVF and important element to assess one's fertility [39].

The volume of ovary and number of follicles are closely related to OR function; the decreasing volume of ovary and decreasing number of antral follicles indicates the decline of OR function. However, the diagnostic value of ovarian volume index is controversial, as its normal volume is between 2.47~7.75 cm^3, which is of great variation. If the threshhold is 2 cm^3, the volume of the ovary has decreased before the upsurg of FSH. The volume of ovary is the independent predictive factor of the number of acquired oocyte; its sensibility and specificity are equally 75% [40].

At present, there are different kinds of indexes used in the study of mesenchymal blood of ovary, such as peak systolic velocity (PSV), pulsation index, resistance index, vascularization index, discharge index, *etc.*; however, all cannot be easily compared with each other. In light of the

connection between mesenchymal blood and OR or IVF reactivity, we can predict its potential in the prediction of menopausal age and OR evaluation. It can be classified as 0~III. Experts thought that except for the age factor, when the PSV > ten cm/s, the number of mature eggs and rate of pregnancy were kept at a relatively high level [40]. Therefore, the performance of mesenchymal ovarian blood before promoting ovulation could be used as an index to reflect OR function. As a result of lacking researches, a more accurate measure is required to establish a more accurate normal range [41]; furthermore, it is very difficult to perform clinically, so further studies are needed to assess its application value.

Immunity and function evaluation of ovary

Several studies had shown that POF was related to autoimmunity. The connection between autoimmunity and OR is drawing more and more attention. Studies from molecular immunology indicate that 4~10% of POF patients have lymphocytic oophoritis. Because of lacking sufficient evidence and more precise diagnostic tools to determine the pathogenesis (autoimmunity), the detection of all relevant antibodies (autoimmunity) from POF patients is lacking. Currently, most believe that anti-thyroid-globulin antibody (TG-Ab), anti-thyroid peroxidase antibody (TPO-Ab), and anti-adrenocortical antibody (ACA) can be used to perform immunological detection for OR, as well as offer immunological treatment; thus we could ameliorate incipient ovarian failure and transitional ovarian failure and even get our patients recovered from POF completely [24, 41]. Researchers have made remarkable progress in clinical treatment for the POF patient with positive TG-Ab. Their theoretical basis is that POF is reversible and the residual function of follicle may be revived after immune dysfunction, which finds more important value in the stage of incipient ovarian failure and transitional ovarian failure.

ACA is the representative of immunity oophoritis. Autoimmune diseases relevant to POF include diabetes, myasthenia gravis, xerophthalmia, autoimmune polyglandular syndrome (APS), *etc.* ACA can only be a warning sign in evaluating OR and has not reached a quantitative criteria.

The prospective of establishing classification system for ovarian function

It is quite obvious that all the aforementioned indexes capable of predicting OR and reflecting ovarian function cannot sufficiently reflect OR. Therefore research proposed the combination of several indexes to evaluate ovarian function, which is functionally superior to any single index. Oliveira *et al.* [42] combined the level of serum AMH, number of antral follicles, and age to establish ovarian response prediction index (ORPI). ORPI= (AMH×AFC) /age, 101 cases of ICSI women were involved, and the results showed that there

Table 1. — *Draft of classification system for ovarian reserve function.*

Score	1	2	3	6	10
AMH (ng/ml)	11~12	2~10	1.9~1	0.9~0.5	<0.5
INH-B (ng/L)	70~80	60~59	40~29	30~14	<14
AFC	5	4	3	2	≤1
FSH (IU/L)	8~12	13~20	21~25	26~40	>40
FSH / LH	1.5~1.9	2.0~2.5	2.5~3.0	3.1~3.6	≥3.7
E2 (pmol/L)	290~360	361~510	>510	73~130	<73

Grade I: 1~2, normal; Grade II: 3~8, MT phase;
Grade III: 9~10, early period of menopause;
Grade IV: >10, late period of menopause;
AFC: average value of the bilateral ovary count.

was close connection between ORPI and rate of pregnancy, obtaining eggs and the number of egg during mitosis II; thus, it can be a indicator in predicting ovarian function. This study was an attempt to quantify OR function, however, the authors themselves still believed that it was not sufficiently comprehensive, detailed, and objective.

Classification system for ovarian function

After years of accumulation in clinic and referring to assorted documents, (classification system for fallopian tube function) and (staging of endometriosis by American fertility association), the present authors established classification system of their own based on the currently effective indexes (Table 1).

Definition of different grades
- OR grade I is scored 1~2.The OR is basically normal and should be rechecked after half year.
- OR grade II is scored 3~8. It belongs to the menopausal transition (MT) phase. The patients need to be closely observed and offered treatment when necessary. For those desiring to become pregnant, indications will be given in time and assisted reproduction will be implemented when necessary.
- OR grade III is scored 9~10. Most are in the early period of menopause (within two years after menopause). Hormone replacement treatment (HRT) will be given for those with no contraindications.
- OR grade IV is scored over 10. Most are at the late period of menopause (more than two years after menopause). For these women who have osteoporosis and urogenital system atrophy should be closely monitored and given timely treatments. HRT and calcium supplement should be given under strict observation.

Classification system indications
- Patients with organic diseases, such as hypoplasia of gonads, ovarian arterial embolism, and gynecologic malignant tumor, etc, should not be included in this classification.

– Final confirmation can be reached only after three laboratory reports with at least one month interval. Because the decline of ovarian function in the same individual is complex, hence the examination is needed to be performed at least twice, and even several times in order to evaluate comprehensively.

– Although the influence to AMH and AFC is not extensive when taking oral contraceptives, it can reduce FSH, LH, and E2. Therefore ovarian function evaluation is given three months after drug withdrawal. For other steroid hormones used, the evaluation should be performed one month after the drug withdrawal.

– Interventional treatment of ovarian cyst is likely to have effects on ovarian function, hence evaluation is given three months after treatment.

High-risk group

– The events occur twice or more within six menstrual cycles: the menstrual duration is altered (> seven days or more different with normal menstrual cycle); or menstrual cycle is no more than 21 days (oligomenorrhea).

– Women older than 38 years of age affected with joint and muscle pain, discomfort, fatigue, insomnia or with any unexplained causes.

– Women with autoimmune diseases, such as Sjogren's syndrome, Hashimoto's thyroiditis with high level TPO-Ab (> 1,000 IU/ml) and rheumatic or rheumatoid arthritis.

– Family history of diabetes or only existence of insulin resistance; although many years after menopause, some of these patients may have higher levels of estrogen accompanied by metabolic syndrome. So the patients should be followed up closely to prevent endometrial lesions and so on.

– Family history of POF.

– At least twice operations history of ovarian or fallopian tube surgeries; hysterectomy performed more than five years ago.

– Patients who suffer anxiety disorder, obsessive-compulsive disorder, and other mental illness requiring antipsychotic drug treatment.

– History of active tuberculosis (TB).

Conclusions

The present authors are first to devise the concept of classification system for ovarian function, which is of great significance for the following reasons: 1) quantitative evaluation of ovarian function can be used in guiding clinical diagnosis and treatment; 2) the classification system can be used in instructing family planning; 3) it can be an early warning sign of ovarian decline; 4) it can help in determining the proper time for performing HRT or ET, as well as in evaluating the effect of treatment; 5) effective system is able to predict the menopausal age; 6) this system can instruct how to treat the diseases of the women in per-

imenopausal period combined with myoma of uterus, adenomyosis, etc. If their ovaries have a high grade of function, they are anticipated to enter menopause in the upcoming one or two years, thus are free from operative treatment; 7) objective system can instruct ART, such as evaluation reaction rate and cancellation rate of ovary, and so on. It is of great help in enhancing pregnancy rate and live-birth rate.

The feasibility of this classification system is waiting to be verified and improved in the future. At present, what the authors have accumulated through clinical assessments has been used in instructing ART and operations. They hope to improve this system step-by-step through continuous clinical practices, making it a more scientifically effective in the foreseeable future. Further studies will be published within in the next two years.

Acknowledgments

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Address reprint requests to:
YU-LAN MU, PhD.
Department of Obstetrics & Gynecology
Shandong Provincial Hospital Affiliated to
Shandong University
324 Jing Wu Road,
Jinan 250021, Shandong (China)
e-mail: mulanxing@hotmail.com